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NovaFlow – Novel applications of a state-of-the-art oscillatory flow platform: hydroxyapatite production and its use in bone extracellular matrix growth

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Hydroxyapatite (HAp) $Ca_{10}(PO_4)_6(OH)_2$ is of significant interest in biomedical engineering due to its exceptional biocompatibility, bioactivity and osteoconductivity properties [1].

In this context, the present project aims at synthesizing HAp crystals with a carefully controlled size, with a controlled and narrow size distribution and with a high purity. Thus HAp crystals shall be produced with a high specific surface area, i.e. small crystals, and a high biocompatibility, making them suitable for application in bone substitution.

The work should start by the characterization of HAp precipitation process, namely by the definition of the optimal operation conditions and the modelling of the process. First, the study will be conducted in a stirred tank. Once the system characterized, HAp precipitation will be carried out in a novel OFR developed by CEB-UMinho [2]. In fact, the OFR appears as a good candidate to promote ideal conditions, in particular in terms of micromixing, for the controllability of HAp particles properties. The effect of some additives with well defined roles in HAp precipitation will also be investigated. In parallel, the biocompatibility of the products developed will be evaluated, by determining the cytoxicity using cell lines (osteoblasts). Finally, the novel OFR will be tested for bone related cells culture, both in the absence and in the presence of HAp crystals.

Initial experiments were performed in a 1L stirred tank, mixing a saturated solution of calcium with a solution of phosphate using different Ca/P molar ratios always at T=37ºC. After process optimization, a suspension of stoichiometric HAp particles with pH close to 7 was obtained for Ca/P=1.29. The particles formed possess a rod-like shape with dimensions of about 20 nanometers thick and 100 nanometers long, and proved to be high crystalline. In addition, HAp crystals revealed the tendency to aggregate in solution and had a narrow size distribution with a mean particle size of about 128 nm.

References

[1] Oliveira C, Ferreira A and Rocha F, "Dicalcium phosphate dihydrate precipitation, characterization and crystal growth", *Chemical Engineering Research and Design* (2007) **85**:1655-1661.

[2] Reis N, Vicente AA, Teixeira JA, Mackley MR, "Residence times and mixing of a novel continuous oscillatory flow screening reactor", *Chemical Engineering Science* (2004) **59**:4967-4974.